Risk factors for community acquired urinary tract infections caused by extended spectrum β-lactamase (ESBL)

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Tabla de contenido

Abreviation

Urinary tract infection UTI

Extended-spectrum β-lactamases ESBLS

Multi-drug Resistance MDR

United States of America USA

Ureteropelvic Junction Obstruction UJO

Penicilin PCN

trimethoprim sulfamethoxazole TMP-SX

White blood count WBC

Minimum inhibitory concentration MIC

1. Introduction

Urinary tract infections are an important source of consults and admissions, they can increase morbidity, hospitalization stay and have serious consequences to the future life like chronic kidney damage, hypertension, renal scars(1)(2); that is why the importance of a promptly and appropriate treatment to avoid those complications.

There is an increased resistance to antibiotics, one of the common mechanism of resistance is the production of ESBLS that are hydrolyzing enzymes produced as a resistance mechanism by Enterobacteriaceae, those enzymes have an important role in health issues because they are widespread and confer resistant to many antibiotics that are commonly used in the clinical settings like cephalosporins, penicillin's; lose the useful of this important antibiotics is a Hugh concern mostly in pediatric medicine, where antibiotics option are more limited than adults.(3)(4)(5)

The ESBL bacterias have been found often in the hospital setting causing infections during the stay in the hospital, but recently there have been an increased in the cases of ESBL infections in the community setting(6)(7) so is important to know what are the risk factors so to prevent ones that can be preventable and be aware those that are not preventable

2. Problem Statement

There has been a great concern about resistance in the past years, the worldwide spread of ESBLS bacteria, principal *Escherichia coli* have made clear the importance of development of new therapies against MDR bacteria. In the past decade the detection of CTX-M types ESBLS-producing E. coli in the community have been growing.(8)

A global surveillance database in Europe has shown a flat trend of 15 – 30% in the detection of ESBL bacteria, North America rates were10% and the nosocomial rates in USA have been increasing 7.8% in 2010 and 18.3% in 2014.(9)(10). The increased in community ESBL bacteria has also been addressed by the literature, a meta-analysis show the colonization with this bacteria, the global average rate was 14%, in South, Southeast, and East Asia, the rates were 50% and in USA and Europe there were 10%.(11) UTI represent the second most common infection in children, the most common organism is E. Coli, (12)

The UTI in pediatric population create a Hugh concern because the consequences of renal damage and development of chronic renal disease and hypertension, that is why is so important to guarantee an adequate treatment, as noticed previously because of the increased of ESBL bacteria there is a risk that the empiric treatment don't be the adequate, for that this study focus in knowing the risk factors of this infection to contribute in the prevention and also the knowledge of the clinicians when they decided a specific therapy for the patient (12)

Studies of the risk factors associated with ESBL-producing G-ve infections in children have mainly focused on hospitalized children [10, 11]. However, few recent studies of community acquired ESBL infections in children are published. Topaloglu et al found that having an underlying disease and hospitalization within the last 3 months were potential risk factor for infection with ESBL-producing E coli and Klebsiella in children [12]. Previous exposures to antibiotics and young age (< 1 year) have also been demonstrated to be risk factors in additional studies [13]. However, these studies were done in countries with known high prevalence of ESBL infections or in medical centers that use cephalosporins in antibiotic prophylaxis. Recent studies have shown that the rates

of ESBL infections in children in the USA are increasing [14]. However, the risk factors of ESBL-producing bacteria in the community acquired UTI in children in the USA remain unclear.

In recent years, an increasing number of children with community acquired (CA)-UTI due to ESBL-producing organisms, especially E. coli, has been observed at our institution. The primary aim of this study was to determine the frequency of CA-UTIs caused by ESBL-producing bacterial pathogens in children seen at Children's Hospital of Michigan during 2012-2016 and investigate the characteristics of children to determine the risk factors associated with these infections.

This problem makes the following question

¿What were the risk factors for development of ESBL UTI in children that where seen in Children Hospital of Michigan since 2012 to 2016?

3. Justification

This investigation pretend to know the risk factors associates with ESBL E. Coli UTI so that can be create strategies to avoid and prevent those factors, also planning for control of antimicrobial resistance.

The data obtained can be compared to results that were obtained around the world and also can contribute to the management of the patients in communities that are similar to the community that was evaluated

4. Background

4.1 Epidemiology

Urinary tract infection is a important problem in childhood, that led to complications if don't received acceptable treatment. The prevalence of UTI in children is approximately 7% in febrile infant, but varies regarding age, sex, ethnicity. There is a higher prevalence in uncircumcised boys, white children have higher prevalence than black children, girls have higher prevalence that boys(13)(14)

4.2 Microbiology

Escherichia coli is the most common bacterial cause of UTI, accounts for approximately 80%. There are other microorganism like Klebsiella, Proteus, also Gram positive organism like Staphylococcus saprophyticus or Enterococcus(15), viral and fungal infection is also reported.

4.3 Pathogenesis

The source of infection in pediatric above new born is a result of ascending infection, that have been probed in studies that documented only 4-9% of children with UTI are bacteremic(16)

The firs step to develop a UTI is the colonization of the paraurethral area, those bacteria attach to the uroepithelial cells on the glycosphingolipid receptors on the surface of

epithelial cells, that attachment recruit TLR, this biding taggers a cytokine response that generates a inflammatory response(17)
The E coli has some virulence factors like pili, hair-like appendages on the cell Surface, with those can adhere to the uroepithelium and ascend into the kidney where create a inflammatory response that can lead to a scar(17)

There have been described factors associated to this infection like the age which is highest in boys younger than one year and girls younger than four years, also lack of circumcision(18), increased prevalence in woman UTI, urinary obstruction that can be generated by a anatomic or functional problem(19), Vesicoureteral reflux VUR is the retrograde passage of urine from the bladder into the upper urinary tract. It is the most common urologic anomaly in children. Children with VUR are at increased risk for recurrent UTI. (2)
Clinical presentation
UTI symptoms in infant and young children are unspecific, the most common symptoms are fever, the presence of fever without other source of infection is a good predictor of UTI, the past medical history of UTI and lack of circumcision is helpful to think of UTI diagnosis(20), other symptoms that are less common are poor feeding, failure to thrive, irritability. In older children the presence of dysuria, frequency, flak pain is suggestive of pyelonephritis. (21)

4.4 Clinical evaluation
The risk of renal scarring was increased with increasing duration of fever before initiation of antibiotics so the prompt recognition and treatment of UTI is very important to prevent the bad consequences. (22)

Some of the risk factors that have been addressed are bladder dysfunction, chronic constipation, previous UTI, VUR, family history of UTI or VUR or other genitourinary abnormalities, antenatally diagnosed renal abnormality, used of barrier contraception with spermicidal agents. (16)

4.5 Physical examination

The vital signs can show fever, is important to access the blood pressure if is Hight it would be a indication of chronic recurrent UTI also poor weight gain and failure to thrive, positive findings that can indicated UTI are abdominal tenderness, suprapubic tenderness, costovertebral tenderness, a sign of acute UTI.(23)

4.6 Laboratory Tests

The laboratory tests for a child with UTI are a urine simple for a dipstick and microscopic evaluation

Urine sample

The decision to obtain a urine sample for culture is best made on a case-by-case basis, taking into consideration the age, sex, circumcision status, and the presenting signs and symptoms

Urine culture is the standard test for the diagnosis of UTI. Can be performed routinely for all children in whom UTI is a diagnostic consideration and in whom a sample for urinalysis or dipstick is collected

A meta-analysis of individual patient data from nine studies including 1280 children (0 to 18 years) who underwent renal scintigraphy at least five months after their first UTI found that polymorphonuclear count >60 percent and CRP >40 mg/L were associated with increased risk of renal scarring [19]. However, the blood tests contributed only minimally when added to models for predicting renal scarring that included temperature, etiologic agent, and renal bladder ultrasonography and/or voiding cystourethrogram.

4.6 Diagnosis of UTI

Overview — Quantitative urine culture is the standard test for the diagnosis of UTI. UTI is best defined as significant bacteriuria in a patient with pyuria (ie, evidence of an inflammatory response). If the urine culture demonstrates significant growth of

Enterococcus, Klebsiella, or Pseudomonas aeruginosa in a child with symptoms of UTI, UTI may be diagnosed in the absence of pyuria

Significant bacteriuria — What constitutes significant bacteriuria depends upon the method of collection and the identification of the isolated organism. Lactobacillus spp, coagulase-negative staphylococci, and Corynebacterium spp are not considered clinically relevant uropathogens [22].

Significant bacteriuria from a clean voided urine specimen in children as growth of ≥100,000 colony forming units (CFU)/mL of a single uropathogen; a second uropathogen with growth <50,000 CFU/mL is permitted, but a higher colony count for the second uropathogen or growth of multiple organisms is considered contamination.

Significant bacteriuria from catheterized specimens in children as growth of ≥50,000 CFU/mL of a single uropathogen [22,42]; a second uropathogen with growth <10,000 CFU/mL is permitted, but a higher colony count for the second uropathogen or growth of multiple organisms is considered contamination. In a prospective study of febrile children <24 months of age, catheterized urine samples with 10,000 to 50,000 CFU/mL were more likely than specimens with ≥50,000 CFU/mL to yield gram-positive organisms (excluding enterococci) or mixed organisms (65 versus 17 percent)

4.7 ESBL

Extended-spectrum β lactamases (ESBLs) are β-lactamases that hydrolyze extended-spectrum cephalosporins with an oxyimino side chain. These cephalosporins include cefotaxime, ceftriaxone, and ceftazidime, as well as the oxyimino-monobactam aztreonam. Thus ESBLs confer resistance to these antibiotics and related oxyimino-β lactams [1, 2].

5. Objectives

- Identify the risk factors for development community acquired urinary tract infections caused by extended spectrum β-lactamase (ESBL)

- Describe the clinical characteristics of the groups
- Determine the relation or association with the clinical presentation and the results
- Identify the treatment used for UTI
- Identify the resistance parameters of the bacteria that caused UTI by ESBL E. coli and Non ESBL E. coli

6. Methodology

Children who presented to our hospital with CA-UTI due to ESBL-producing E. coli during the period January 2012 - January 2016 were included in the study. The Children's Hospital of Michigan is a 220-bed tertiary care center in Detroit, Michigan. Urine cultures that were positive for ESBL-producing E. coli were identified from the records of the University Microbiology Laboratory of the Detroit Medical Center. A control group consisting of children with UTI caused by non-ESBL-producing E. coli was included. Patients in the control group were matched by age, gender, and year of the CA-UTI due ESBL-producing E. coli group.

Exclusion criteria included positive urine cultures >72 hours after hospitalization, patients with long term care facility stay within the preceding 3 months, postoperative infections within 10 days of surgery, and asymptomatic bacteriuria.

Each urine culture was included once in the study. If more than one positive ESBL-producing E. coli urine culture was present, the last clinical record with the least missing data was included. Positive urine culture was defined according to the method of collection of the urine sample. Bag specimens were not included in the analysis. In midstream specimens of urine, UTI was defined as a positive urine culture ≥105 CFU/mL or a positive urine culture (104 - 105 CFU/mL) with pyuria of ≥10 leukocytes per high power field. In specimens obtained through by bladder catheterization, growth of 104 - 105 CFU/mL was defined as UTI.

Medical records of patients with UTI caused by ESBL-producing and non-ESBL producing E coli were reviewed to obtain information on demographic characteristics, history of hospital visits, clinical findings, urine culture pathogen its antimicrobial susceptibilities, laboratory and imaging studies, comorbidities, treatment modalities, hospital course, complications, and outcome. Information was collected and analyzed for the following potential risk factors for ESBL infection: history of previous UTI, anatomic abnormalities of the urinary tract, antibiotic usage in the past 3 months, previous hospitalizations, intensive care unit stay, surgeries, underlying neurologic abnormalities such as spina bifida or neurogenic bladder, previous infections, history of infection with ESBL-producing bacteria or other resistant bacteria, and intermittent urinary bladder catheterization.

6.5 Variables

Table 1.

Variable	***Definition***	***Codification***	***Type***
Demographics			
Age	Live time of a person	Numbers	Cuantitative
Gender	Biological and physiological characteristics that define men and women	Female Male	Cualitative nominal dicotómic
Length of stay	Time of stay during the episode	Numbers	Cuantitative
Lengh of stay previouss to culture	Time of stay p previous to the culture	Numbers	Cuantitativa de razón
Race	Grouping of humans based on shared physical or social qualities into categories generally viewed as distinct by society.	Black, Caucasian, Hispanic, Arabic, Other	Cualitative
Clinical presentation			

Fever	Abnormally high body temperature above 38 C	Números absolutos	Cuantitativa de razón
Vomiting	Act or instance of disgorging the contents of the stomach through the mouth	Yes/ No	Cualitative nominal dicotómic
Dysuria	Painful urination.	Yes/ No	Cualitative nominal dicotómic
Enuresis	Involuntary urination	Yes/ No	Cualitative nominal dicotómic
Gross hematuria	Blood in the urine that can be seen	Yes/ No	Cualitative nominal dicotómic
Change in color of the urine	Change in the color of the urine	Yes/ No	Cualitative nominal dicotómic
Change in smell of the urine)	Change in smell of the urine	Yes/ No	Cualitative nominal dicotómic
Abdominal Pain	Pain in the abdomen	Yes/ No	Cualitative nominal dicotómic
Flank Pain	Pain in the flank	Yes/ No	Cualitative nominal dicotómic
Restless	Unwilling or unable to stay still or to be quiet and calm	Yes/ No	Cualitative nominal dicotómic
Low appeitite	Low appeitite	Yes/ No	Cualitative nominal dicotómic
Diarrhea	Loose, watery stools three or more times a day.	Yes/ No	Cualitative nominal dicotómic

History of infection (last 3 months)	Any infection in the last three months previous to the UTI	Yes/ No	Cualitative nominal dicotómic
History of UTI (last 3 months)	Diagnosis of UTI in the last three months	Yes/ No	Cualitative nominal dicotómic
ESBL UTI	History of ESBL UTI in the last three months	Yes/ No	Cualitative nominal dicotómic
History of Hospitalization last 3 months	Any hospitalization in the last three months	Yes/ No	Cualitative nominal dicotómic
History of Hospitalization last 3 months for renal causes	Any hospitalization in the last three months for renal causes	Yes/ No	Cualitative nominal dicotómic
History of Prior surgeries last 3 months	History of Prior surgeries last 3 months	Yes/ No	Cualitative nominal dicotómic
Intraurinary tract device (Catheter, 2=ureteral stents)	Presence of any intraurinary tract device	Yes/ No	Cualitative nominal dicotómic
Duration of intraurinary tract device	Time since the start with the urinary tract device	Numbers	Cuantitative
Intraurinary tract intervention	*Intraurinary tract intervention*	Yes/ No	Cualitative nominal dicotómic
Underlying diseases	Presence of any of this Myelomenigocele, GU	Myelomenigocele, GU abnormality,	Cualitative

	abnormality, Other, Combination	Other, Combination	
VUR	Presence of vesicoureteral reflux	Yes/ No	Cualitative nominal dicotómic
Urinary abnormalities	*Presence of any urinary abnormalities*	Hydronephrosis, UPJO,Duplex Systems, Multiple anomalies, other, phimosis	Cualitative
Functional Abnormalities	*Presence of any of this functional abnormalities*	*Neurogenic bladder, voiding dysfunction, both, constipation)*	Cualitative
Nephrolithiasis/calcinosis	*Presence of any of Nephrolithiasis/calcinosis*	Yes/ No	Cualitative nominal dicotómic
Recurrent UTIs without renal anomaly	Diagnosis of more than one UTI in the past *without renal anomaly*	Yes/ No	Cualitative nominal dicotómic
Sepsis	Presence of signs and symptoms of inflammation and evidence or suspicion of microbial process	Yes/ No	Cualitative nominal dicotómic
Systemic Diseases	Diagnosis of any other medical problem like oncologic, metabolic, other	Yes/ No	Cualitative nominal dicotómic
Immunosuppressed	Reduction of the activation or efficacy of the immune system	Yes/ No	Cualitative nominal dicotómic
History of antibiotic usage last 3 months	Used in the last 3 months any antibiotic	Yes/ No	Cualitative nominal dicotómic
Antibiotic class	*Type of antibiotic used in the last 3 months*	*PCN, cephalosporin, TMP-SMX, Nitrofurantion, Combinations, Other*	Cualitative

Prior Beta-lactam use	Used of any *Beta-lactam antibiotic in the last three months*	Yes/ No	Cualitative nominal dicotómic
Intravenous Treatment of ESBL UTI	Antibiotic administered into a vein or veins.	Yes/ No	Cualitative nominal dicotómic
PO treatment	treatment that is taken orally	Yes/ No	Cualitative nominal dicotómic
Duration	time from the start and end of the antibiotic	Numbers	Cuantitative
Adequate Treatment - current antibiotic for majority of course	The antibiotic that was used was sensitive to the organism	Yes/ No	Cualitative nominal dicotómic
Surgical Intervention	Procedure performed during the infection	Yes/ No	Cualitative nominal dicotómic
Clinical outcome	Results,	Resolution, unknown, recurrent UTI	Cualitative
Complications			
Complication	After the UTI presence of any of the following	AKI, Recurrent UTI, Kidney Abscess	Cualitative
Positive Blood culture	Isolation of microorganism in blood culture	Yes/ No	Cualitative nominal dicotómic
Infection other sites	Precense of infection in other place than the urinary tract	Yes/ No	Cualitative nominal dicotómic
Mortality within 1 yr of diagnosis	Death within 1 yr of diagnosis of UTI	Yes/ No	Cualitative nominal dicotómic
Physical Findings			
Abdominal Pain	Pain of the abdomen during the examination	Yes/ No	Cualitative nominal dicotómic
Flank Tenderness	Discomfort, distress, or agony in the part of the body below the rib and above the ilium, generally beginning posteriorly or in the midaxillary line	Yes/ No	Cualitative nominal dicotómic

Suprapubic Tenderness	Discomfort, distress, or agony in the suprapubic area during the examination	Yes/ No	Cualitative nominal dicotómic
Laboratory Data			
WBC	white blood cell count	Numbers	Cuantitative
Diff (Neutrophils)	Leucocyte having a lobed nucleus and a fine granular cytoplasm, which stains with neutral dyes that destroy bacterias	Numbers	Cuantitative
Diff (Bands)	WBCs are first released from the bone marrow into the peripheral blood	Numbers	Cuantitative
Diff (Lymphocytes)	Leucocyte that destroy viral pathogens	Numbers	Cuantitative
Diff (Monocytes)	Type of leukocyte that play a role in the immune response	Numbers	Cuantitative
Diff (Eosinphils)	Type of leukocyte	Numbers	Cuantitative
Hgb	Protein that carries oxygen	Numbers	Cuantitative
Hct	Percentage of red blood cells in blood.	Numbers	Cuantitative
Platelets	Component of blood whose function is to react to bleeding from blood vessel injury by clumping	Numbers	Cuantitative
BUN	Blood urea nitrogen amount of nitrogen in urea form that circulates in the blood	Numbers	Cuantitative
Cr	Creatinine – protein that is filtrated in the kidney and evaluated the renal function	Numbers	Cuantitative
CRP – C reactive protein	Blood test marker of inflamation	Numbers	Cuantitative
ESR erythrocyte sedimentation rate	*A blood test that detects and monitors inflammation in the body*	Numbers	Cuantitative
Urine Specific Gravity Test	Compares the density of urine to water	Numbers	Cuantitative

UA WBC	Presence of white blood cell in the urine	Numbers	Cuantitative
UA RBC	Presence of red blood cell in the urine	Numbers	Cuantitative
UA LE	Presence of white blood cell in the urine	Numbers	Cuantitative
UA Bacteria	Presence of bacteria in the urine	Numbers	Cuantitative
Colony Count (CFU) of E. coli	Numbers of colony of E. coli in the urine	Numbers	Cuantitative
2nd Colony CFU (if present)	Numbers of colony of other bacteria in the urine	Numbers	Cuantitative
2nd Colony Bacteria	What other class of bacteria is found in the urine	Non-ESBL E. coli,ESBL e. coli, ESBL Klebsiella, GBS, Non-ESBL Klebsiella, enterococcus faecalis, mixed flora, Hafnia Alvei	Cualitative
Amikacin minimum inhibitory concentration	The lowest concentration of amikacin which prevents visible growth of a bacterium	Numbers	Cuantitative
Amikacin sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Ampicilin sulbactam minimum inhibitory concentration	The lowest concentration of *Ampicilin sulbactam* which prevents visible growth of a bacterium	Numbers	Cuantitative
Ampicilin sulbactam Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Ampicilin minimum inhibitory concentration	The lowest concentration of *Ampicilin* which prevents visible growth of a bacterium	Numbers	Cuantitative
Ampicilin Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Aztreonam minimum inhibitory concentration	The lowest concentration of *Aztreonam* which	Numbers	Cuantitative

	prevents visible growth of a bacterium		
Aztreonam Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Cefazolin minimum inhibitory concentration	The lowest concentration of *Cefazolin* which prevents visible growth of a bacterium	Numbers	Cuantitative
Cefazolin Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Cefepime minimum inhibitory concentration	The lowest concentration of *Cefepime* which prevents visible growth of a bacterium	Numbers	Cuantitative
Cefepime Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Cefoxitin minimum inhibitory concentration	The lowest concentration of *Cefoxitin* which prevents visible growth of a bacterium	Numbers	Cuantitative
Cefoxitin Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Cefotaxime minimum inhibitory concentration	The lowest concentration of *Cefotaxime* which prevents visible growth of a bacterium	Numbers	Cuantitative
Cefotaxime Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Ceftriaxone minimum inhibitory concentration	The lowest concentration of *Ceftriaxone* which prevents visible growth of a bacterium	Numbers	Cuantitative
Ceftriaxone Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Ciprofloxacin minimum inhibitory concentration	The lowest concentration of *Ciprofloxacin* which	Numbers	Cuantitative

	prevents visible growth of a bacterium		
Ciprofloxacin Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Ertapenem minimum inhibitory concentration	The lowest concentration of *Ertapenem* which prevents visible growth of a bacterium	Numbers	Cuantitative
Ertapenem Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Gentamicin minimum inhibitory concentration	The lowest concentration of *Gentamicin* which prevents visible growth of a bacterium	Numbers	Cuantitative
Gentamicin Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Meropenem minimum inhibitory concentration	The lowest concentration of *Meropenem* which prevents visible growth of a bacterium	Numbers	Cuantitative
Meropenem Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Imipenem minimum inhibitory concentration	The lowest concentration of *Imipenem* which prevents visible growth of a bacterium	Numbers	Cuantitative
Imipenem Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Nitrofurantoin minimum inhibitory concentration	The lowest concentration of *Nitrofurantoin* which prevents visible growth of a bacterium	Numbers	Cuantitative
Nitrofurantoin Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Piperacillin/Tazobactam minimum inhibitory concentration	The lowest concentration of *Piperacillin/Tazobactam*	Numbers	Cuantitative

	which prevents visible growth of a bacterium		
Piperacillin/Tazobactam Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Bactrim minimum inhibitory concentration	The lowest concentration of *Bactrim* which prevents visible growth of a bacterium	Numbers	Cuantitative
Bactrim Sensitivity	Sensitivity of the antibiotic sensitive or resistance	Yes/ No	Cualitative nominal dicotómic
Radiological Findings			
Imaging at presentation	Any imaging made at presentation of the UTI	Yes/ No	Cualitative nominal dicotómic
Results	Normal findings or anormal findings	Yes/ No	Cualitative nominal dicotómic
Voiding Cytourethrogram	x-ray examination of a child's bladder and urinary tract that uses a special form of x-ray called fluoroscopy and a contrast material.	Yes/ No	Cualitative nominal dicotómic

6.6 Bias and Errors control

All the information will be collected by four of the authors of the present study, after consensus and definition of variables between all parties. The paraclinical equipment is properly calibrated and monitored by the institution's technosurveillance department on a regular basis. Any question of the findings will be disuss by the authors

6.7 Analysis plan

Data on different clinical variables and frequencies will be analyzed using SPSS version 20. A non-parametric Fisher's Exact test will be employ to examine potential differences between study groups on categorical variables. An independent sample T-test will examine mean differences between study groups.

Variables found from univariate factors described above will enter into a binary logistic regression equation to find the best predictors of acquiring infection with ESBL positive bacteria. A p value of <0.05 was considered statistically significant.

7. Ethics

This investigation was reviewed and approved by the IRB (institutional review board), all the authors were approved by the committee

We declare that there are no conflicts of interest related to any of the researchers of this study.

8. Administration

8.1 Schedule

cronograma		2018
N	Actividades	
1	Subject	
2	Question	
3	Justification	
4	Design	
5	Background	
6	Documents	
7	Approval by the chief of the department	
8	Approval by the IRB committee	
9	Review of the data	
10	Data analysis	
11	Elaboration of the manuscript	
12	Finalization	
13	Publication	

8.2 Budget

All resources come from own income, no funding will be received from the University o hospital, the pharmaceutical industry and / or others.

ITEMS	SOURCE		TOTAL
	Finandable	**No Finandable**	
Personal	No Finandable	No Finandable	**0**
Equipments	300.000	300.000	600.000
Software	250.000	250.000	500.000
Materials	100.000	50.000	150.000
Bibliography	100.000	150.000	250.000
Publication	No Finandable		
Technical service	500.000	500.000	1.000.000
Travels	No Finandable		
Administration	No Finandable No Finandable		
1.TOTAL			1.250.000

8. Expected outcome

There is a grow in the resistance of antibiotics in the past years, we think that one of the cause of this resistance is the bad used of the antibiotics, we expected that the patients that had ESBL UTI will be the ones that receive previous antibiotics and have more risk factors.

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